

ICONOGRAPHIC REVIEW / *Neurology*

Posterior reversible encephalopathy syndrome (PRES): Features on CT and MR imaging

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KEYWORDS

Posterior reversible encephalopathy syndrome;
MRI;
Imaging features

Abstract Posterior reversible encephalopathy syndrome (PRES) is a rare but severe condition of the central nervous system. It develops in a variety of clinical settings and it has diverse patterns of expression, which can sometimes make diagnosis difficult. Characteristic features are often demonstrated on computed tomography imaging and/or magnetic resonance imaging, meaning that when there is a suspicious clinical picture, this diagnosis should suggest itself. However, clinicians should be aware of some of the less typical features in order to more fully understand this condition, in which early treatment is key to good clinical progress.

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Introduction

Posterior reversible encephalopathy syndrome (PRES) is a radiological and clinical entity in which reversible changes occur in the central nervous system, associated with typical features on MR or CT brain imaging. Clinical presentations of this syndrome vary widely as do the imaging features, which may sometimes be atypical. Management may therefore be delayed due to protracted diagnosing or an incorrect diagnosis. The aim of this review of the description and interpretation of imaging findings is to present the various settings in which this condition develops and its patterns of expression, as well as describing the typical and atypical CT and MRI radiological features. This is because in this condition, the clinical picture must be suggestive of the diagnosis, which can then be confirmed by imaging. This means that the factors favouring the development of PRES can be addressed and the inherent complications of a delayed diagnosis can be avoided.

Abbreviations: CT, Computed tomography; MRI, Magnetic resonance imaging; SBP, Systolic blood pressure.

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Table 1 Clinical features of patients with posterior reversible encephalopathy syndrome (PRES).

Settings in which PRES may be likely to develop	Clinical presentations
Arterial hypertension	Headaches
Pre-eclampsia	Confusion
Transplant: allogeneic bone marrow transplant or solid organ transplant	Nausea, vomiting
Immunosuppressant medication: ciclosporin, tacrolimus, etc.	Generalised seizures, sometimes with status epilepticus
Septicaemia, severe infections, often with a state of shock and multiple organ dysfunction syndrome	Cerebellar syndrome
Autoimmune disease: systemic lupus erythematosus, scleroderma, Wegener's granulomatosis	Cortical blindness, hemianopia, blurred vision
Cancer chemotherapy: cisplatin, etc.	Hemiparesis
Chronic renal failure and dialysis	Coma

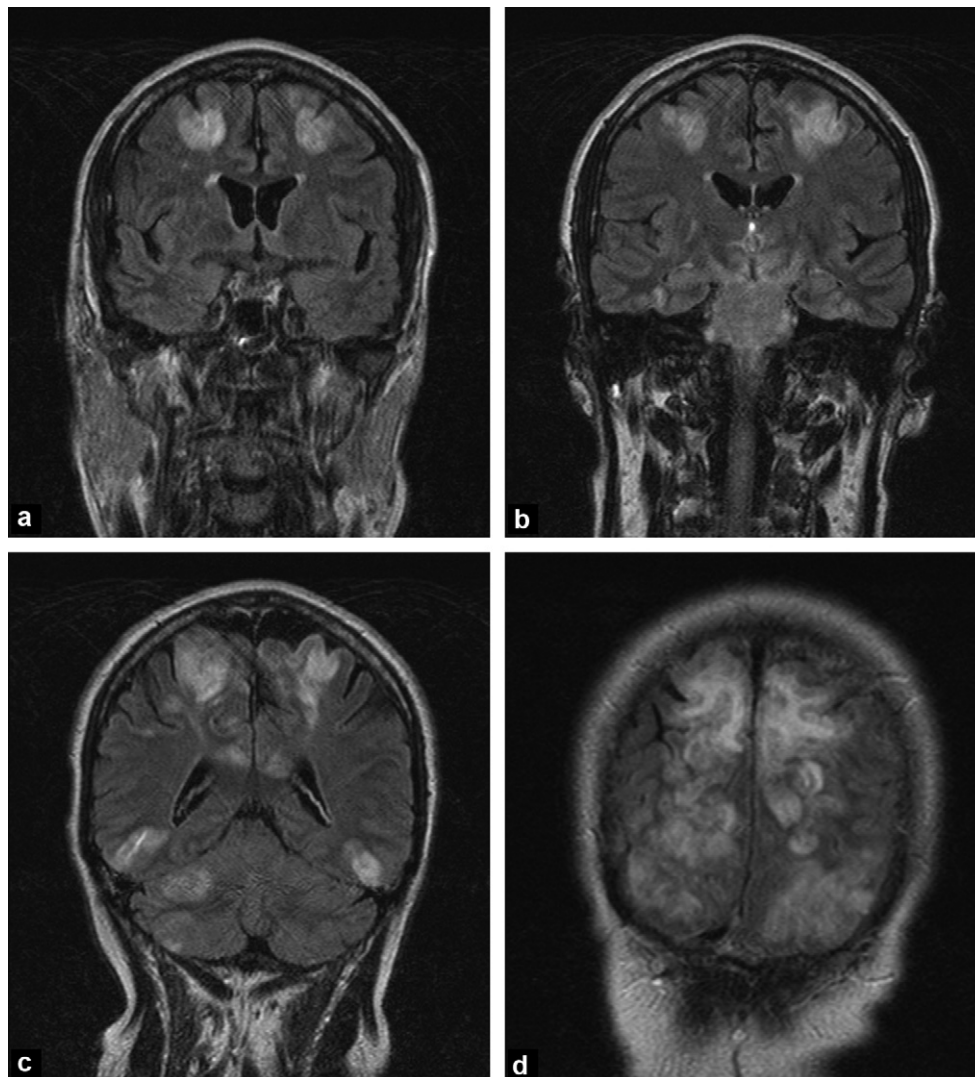


Figure 1. Male aged 36, on dialysis, who had presented static cerebellar syndrome associated with vomiting and drowsiness, preceded by headaches and amaurosis, against a background of hypertension (systolic blood pressure of 200 mmHg). Once his elevated blood pressure had been treated the patient quickly made good clinical progress. The initial MRI showed typical symmetrical holo-hemispheric involvement (FLAIR sequences, coronal views): a: high signal intensity in the frontal lobes; b: high signal intensity in the parietal lobes and the brain stem; c: high signal intensity in the parietal lobes, temporal lobes and cerebellum; d: high signal intensity in the occipital lobes.

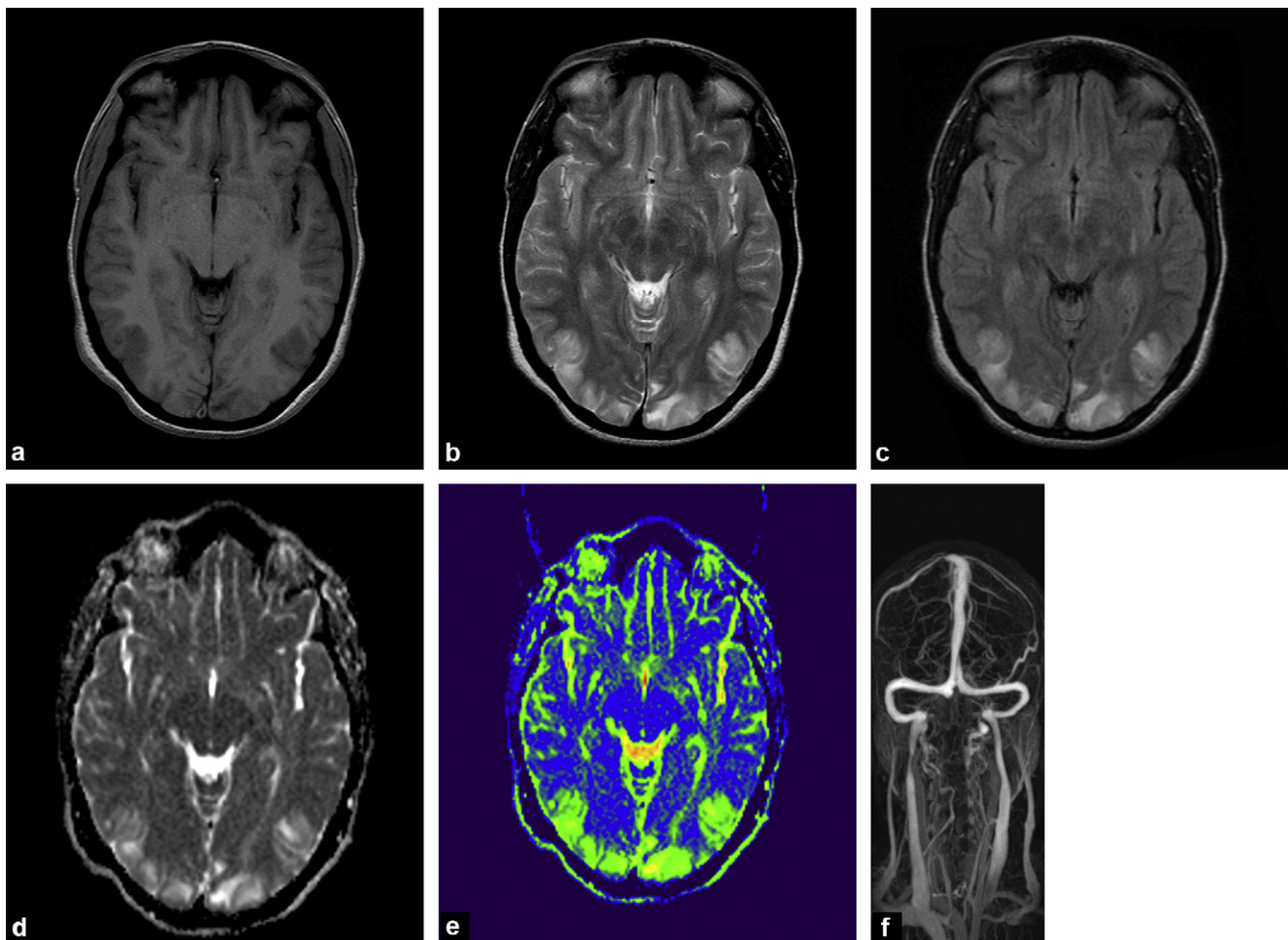


Figure 2. Female aged 31, on dialysis, who had presented with her first partial epileptic seizure against a background of hypertension (systolic blood pressure of 230 mmHg). The MRI showed characteristic diffuse, bilateral, posterior lesions. The neurological signs quickly disappeared after anti-hypertensive treatment: a: T1-weighted axial view: low signal intensity occipital lesions; b: T2-weighted axial view: high signal intensity occipital lesions; c: axial view on FLAIR sequence: high signal intensity occipital lesions; d and e: axial views – diffusion-weighted sequence: the apparent diffusion coefficient mapping in grey and in colour shows high signal intensity from the lesions pointing to a raised diffusion coefficient; f: 3D MR angiography: eliminates the differential diagnosis of cerebral thrombophlebitis by demonstrating that the venous sinuses are patent.

Clinical features

Settings in which posterior reversible encephalopathy syndrome may be likely to develop

There are a number of factors that favour the development of PRES (Table 1):

- arterial hypertension: this is the classic setting and it was the first factor to be described (hypertensive encephalopathy). Moderately to severely elevated blood pressure is reported in 75% of patients [1,2];
- eclampsia or pre-eclampsia: this link has often been drawn [3], even in women with normal blood pressure. Late development of this condition has been reported, as late as several weeks after the birth [3];
- chemotherapy regimens [4] and organ transplants that require patients to use immunosuppressant medications [1,3,5], especially allogeneic bone marrow transplants;

- septicaemia and severe infections, sometimes resulting in organ dysfunction [6];
- chronic renal failure and dialysis [7];
- autoimmune diseases: systemic lupus erythematosus, scleroderma, Wegener's granulomatosis, etc. [8]. This link has often been found, even during periods when patients are not being treated with immunosuppressant drugs.

Clinical presentations

There are a range of neurological presentations that often involve generalised seizures, sometimes complicated by status epilepticus, in combination with headaches, confusion, nausea and vomiting [1,2]. There may be a focal neurological deficit, such as cortical blindness, cerebellar syndrome, or hemiparesis [1,2]. These presentations may lead to coma [1].

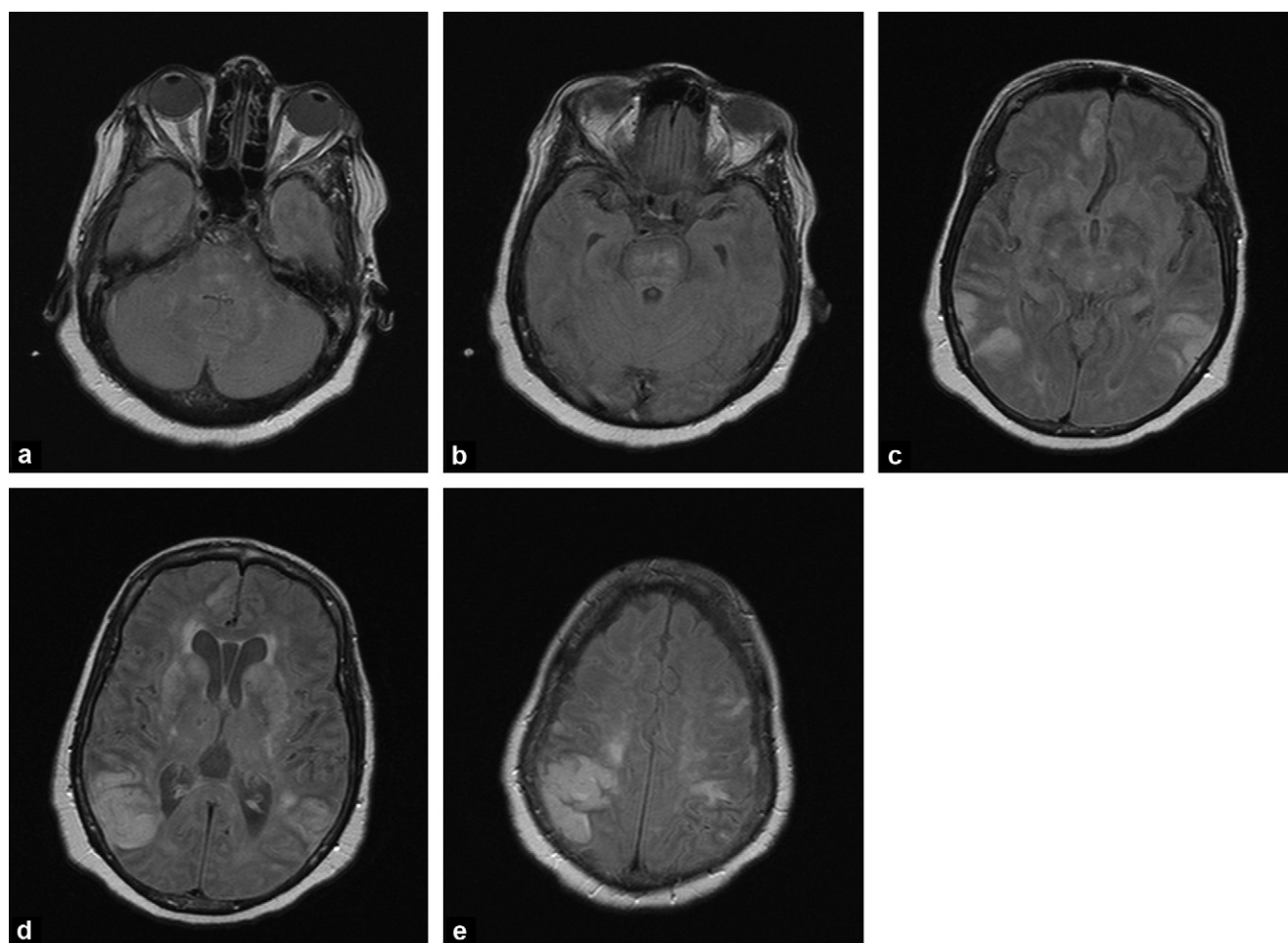


Figure 3. A 55-year-old female who had undergone an allogeneic bone marrow transplant for myelodysplastic syndrome complicated by gastrointestinal graft versus host disease (GVH) treated with ciclosporin. She presented several generalised seizures while in a persistent vegetative state. Ciclosporin was continued in spite of posterior reversible encephalopathy syndrome. Neurological problems including drowsiness, flapping tremor and hyperreflexia persisted intermittently until the death of the patient a few days later, due to complications of GVH. The initial MRI showed a typical holo-hemispheric pattern (axial views in a FLAIR sequence): a: high signal intensity in the cerebellum and temporal lobes; b: high signal intensity in the brain stem; c: high signal intensity in the right frontal sulcus and parietal and occipital regions; d: high signal intensity in the posterior regions of the parietal lobes and the basal ganglia; e: asymmetrical parietal high signal intensity.

Typical imaging features

On imaging, posterior reversible encephalopathy syndrome is characterised by abnormalities of the white matter and the grey matter, predominantly affecting the posterior regions.

Radiological appearance

On computed tomography, diffuse hypodense areas indicate the affected regions. On MRI, lesions appear as iso-intense or low signal intensity on T1-weighted images, and high signal intensity on T2-weighted images and FLAIR. Enhancement is not usually seen after injection of a contrast agent.

Topography

The typical appearance is of diffuse cortical, subcortical and deep lesions. It is usually the posterior regions that

are affected: the parietal or occipital lobes are involved in 98% of cases. However, the lesions can also affect the frontal lobes (68%), the temporal lobes (40%) and the cerebellar hemispheres (30%) [9]. Three major distribution patterns were identified by Bartynski et al. [9]: holo-hemispheric involvement (Fig. 1) in 23% of cases, involvement mainly along the superior frontal sulcus in 27% of cases, and predominantly parietal and occipital involvement in 22% of cases. A bilateral and symmetrical appearance is highly typical although lesions were asymmetrical in 28% of cases.

Diffusion-weighted imaging

On diffusion-weighted imaging, an increase in the diffusion coefficient (Fig. 2) can be seen, connected to the presence of a vasogenic oedema secondary to a dysfunction of the cerebrovascular autoregulation mechanisms. One theory of the mechanism is of a toxic endothelial

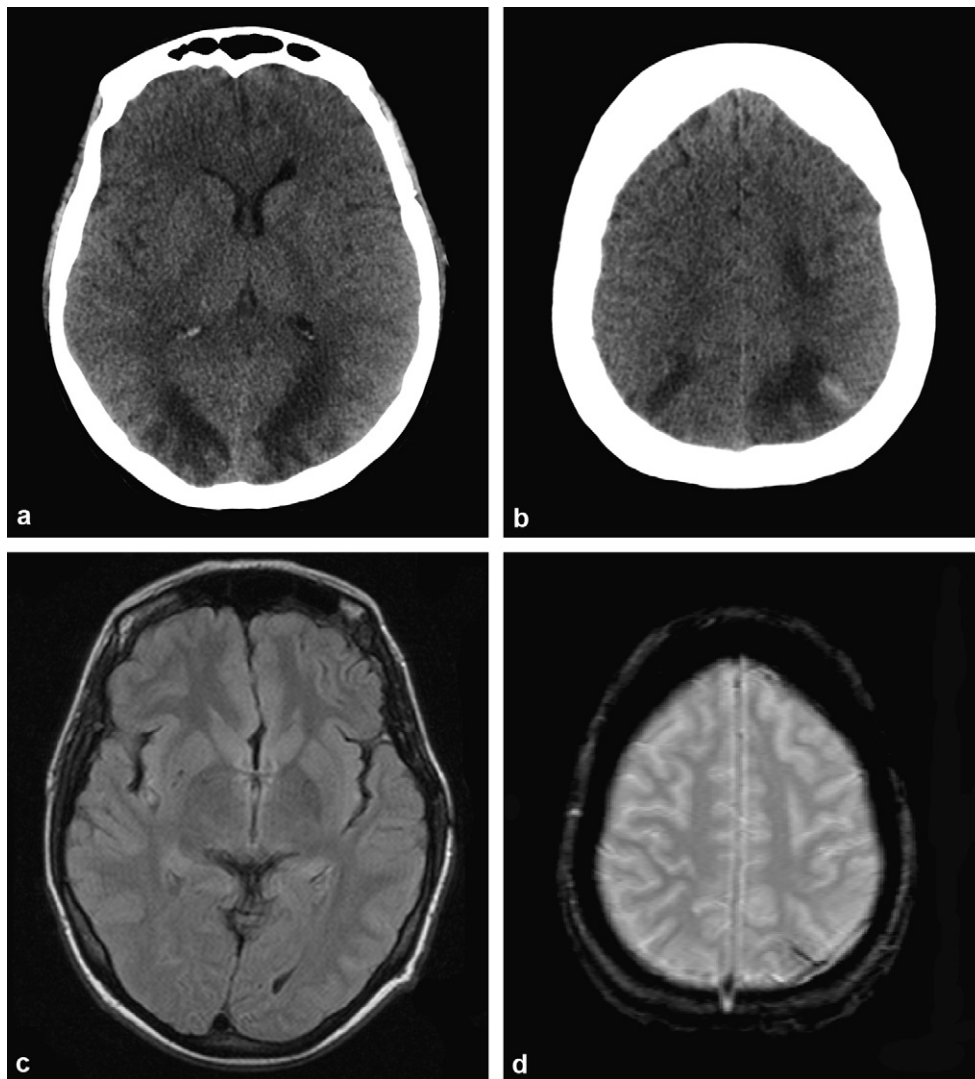


Figure 4. A 34-year-old woman undergoing induction chemotherapy for acute lymphoid leukaemia, treated with intrathecal methotrexate injections, who had presented with sudden right hemiparesis against a background of elevated blood pressure (systolic blood pressure of 200 mmHg). The clinical signs regressed in a few hours: a and b: initial axial view CT without contrast injection showing (a) occipital hypodense areas and (b) bilateral parietal hypodense areas as well as a left parietal haematoma; c and d: axial view MRI repeated after 2 months showing (a) the absence of abnormalities of the residual signal on a FLAIR sequence and (b) left parietal low signal intensity on T2-weighted gradient echo from sequelae of haemorrhage.

dysfunction leading to vasculopathy. The predominance of posterior involvement is explained by the sympathetic nervous system having less significant action on this area, and the sympathetic neurogenic response is supposed to compensate for any deterioration in the myogenic response related to vascular endothelial injury [10]. Given that this vasogenic oedema is reversible, patients normally make good progress after aetiological factors have been addressed.

Angiography and perfusion imaging

Some recent studies have aimed to evaluate lesions in terms of changes on angiography [11,12] in order to identify the mechanisms causing PRES to develop. Angiography demonstrates vascular irregularities with focal and diffuse

vasoconstriction and focal vasodilation often producing a string-of-beads appearance, even in patients without significant hypertension. Perfusion imaging shows a reduction in relative cerebral blood volume, which points to a mechanism involving cerebral hypoperfusion. In addition, vasogenic oedema was less significant in hypertensive patients than in normotensive patients due to a chronic adaptation mechanism of intravascular hyperpressure. These features on angiography suggest that the mechanism causing PRES could begin with endothelial damage leading to vasculopathy, which then causes cerebral hypoperfusion and vasogenic oedema followed by cerebral ischaemia. A protective effect against the spread of lesions could be postulated for hypertension in the acute stage of PRES, in that it allows a sufficient cerebral blood flow to be preserved.

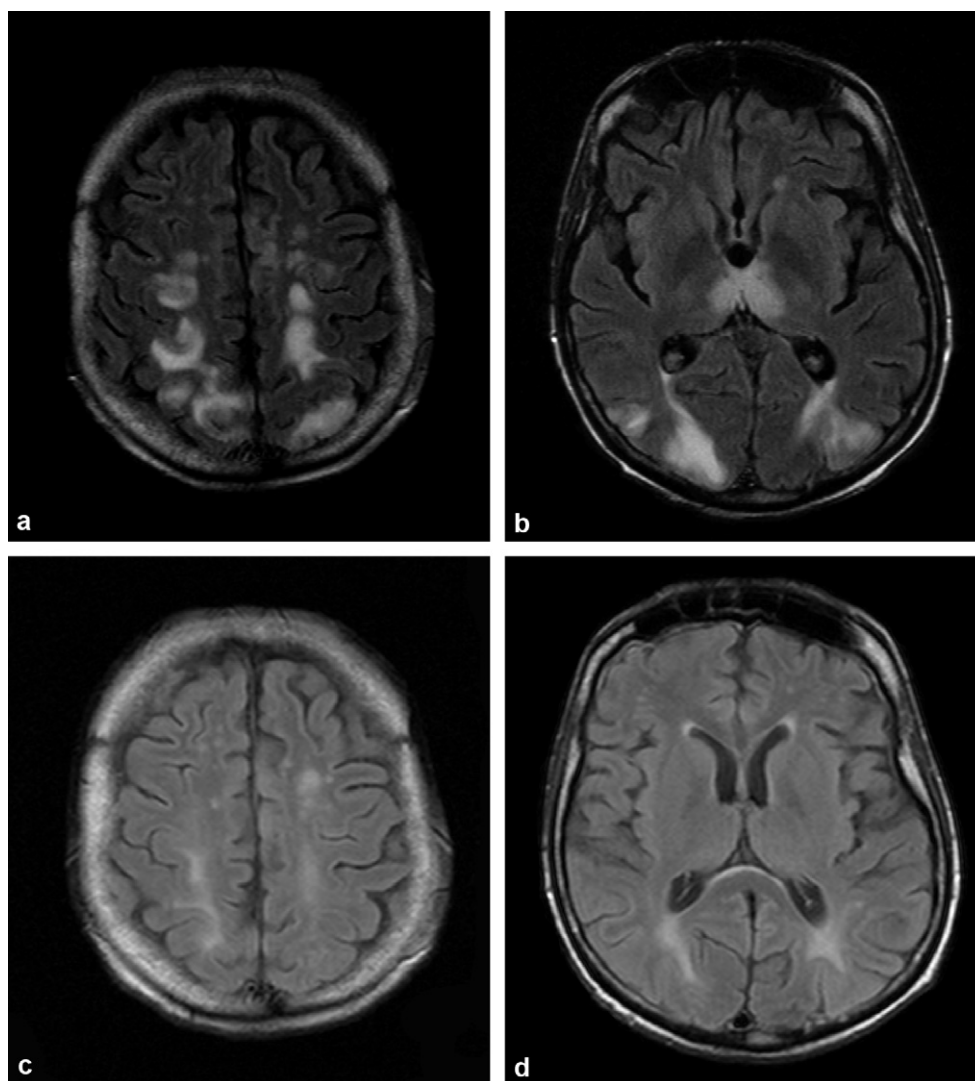


Figure 5. A 51-year-old female, being monitored for dermatomyositis treated with corticosteroids and antiphospholipid syndrome, treated with long-term vitamin K antagonists. She also had chronic renal failure (clearance of 40 mL/min). She had presented with her first two generalised seizures, complicated by status epilepticus. The patient quickly made good clinical progress: a and b: initial axial view FLAIR sequence MRI showing symmetrical high signal intensity in the parietal lobes, occipital lobes and the basal ganglia; c and d: repeat FLAIR sequence MRI of the same plane 17 days later showing that the lesions have significantly regressed.

Atypical presentations

There are some more atypical radiological features that clinicians should be aware of.

In rarer cases, the lesions can extend to the basal ganglia (14%), the brain stem (13%) (Fig. 3) and the deep white matter, in particular the splenium of the corpus callosum (10%) [9]. Even though involvement is unilateral, this must not mean that the diagnosis does not stand.

In some severe forms, the progressive dysfunction of the cerebrovascular regulation mechanisms can cause damage to the blood-brain barrier: in these cases, MRI with gadolinium injection shows enhancement on T1-weighted images [13]. Equally, a cytotoxic oedema may appear, which would show a decreased diffusion coefficient, as in the case described by Benziada-Boudour et al. [14]. In these cases that have progressed further, haemorrhage (Fig. 4) may develop: this happens in between 5 and 30%

of cases, depending on the study [1,15,16]. Three types of haemorrhage have been identified and they have a similar incidence: focal haemorrhage (<5 mm), intra-parenchymal haematoma and sulcal subarachnoid haemorrhage. The risk seems to be greater in patients who have undergone allogeneic bone marrow transplants or organ transplants, as well as in patients taking anticoagulants [16].

Progress

The patient very often makes good clinical progress (Figs. 4 and 5) with clinical signs improving relatively quickly and radiological imaging features soon no longer evident. The condition is usually fully reversible although there remains a risk of neurological sequelae, or even death [17]. Recurrent forms of PRES have been reported: these are cases in which the patient's blood pressure is not satisfactorily

controlled, or when the patient needs to continue taking immunosuppressant drugs (for example, after a transplant) [2].

Differential diagnosis

The main differential diagnoses are [18]:

- acute cerebral ischaemia: unilateral, systematically arranged lesions, with a decreased diffusion coefficient that points to a cytotoxic oedema;
- cerebral venous thrombosis: diffuse, asymmetrical lesions that are sometimes complicated by secondary haemorrhage of the lesion. The diffusion coefficient is raised initially but it can then fall;
- transient cerebral hyperaemia: this can develop after an episode of epilepsy, rapid decompression of a chronic subdural haematoma or an endarterectomy. Diffuse high signal intensity on FLAIR and T2-weighted images point to a vasogenic oedema and the ADC (apparent diffusion coefficient) is raised;
- pontine encephalopathies related to metabolic disorders or mitochondrial encephalomyopathy, lactic acidosis and stroke-like episodes (MELAS) syndrome: lesions are localised to the brain stem, and the ADC is raised;
- autoimmune encephalitis: acute disseminated encephalomyelitis (ADEM). This condition has a distinctive clinical context, often following a viral infection or a vaccination. The MRI may show diffuse high signal intensity on T2-weighted images and FLAIR sequences, which is bilateral but asymmetrical. The ADC is variable: it can be decreased, normal or raised. There is often lesion enhancement, which may be nodular or ring-shaped;
- cerebral oedema in a post-critical condition or after prolonged hypoxaemia: diffuse lesions and a raised diffusion coefficient;
- Creutzfeldt-Jakob disease: lesions with a raised diffusion coefficient, affecting the basal ganglia and the cerebral cortex;
- gliomatosis cerebri: diffusely infiltrating glial tumour with iso-intense or low signal intensity on T1-weighted images and high T2 signal intensity. There is no appearance of necrosis or haemorrhage, nor any initial contrast agent take-up. When present in one or several lobes, this is suggestive of this diagnosis, but when present in isolation in the brain stem, diagnosis can be misled. Spectroscopy demonstrates a tumour-type profile with an increased choline/NAA ratio, and marked elevation of myo-inositol;
- progressive multifocal leukoencephalopathy, against a background of immunosuppression: high signal intensity on T2-weighted images and FLAIR sequences, non-enhancing on T1-weighted images after injection of gadolinium chelates, involving predominantly the subcortical white matter (short fibres) or the parietal and occipital regions. There may be single or multiple lesions, which may be unilateral or bilateral and asymmetrical.

Conclusion

PRES refers to a radiological and clinical syndrome that is characterised by a range of neurological signs appearing

in association with abnormalities of the white matter and the grey matter predominantly affecting the posterior regions. The distinctive clinical context as well as the quick reversibility of the clinical and radiological abnormalities is suggestive of cerebral vasogenic oedema secondary to vasculopathy. Imaging, especially MRI, plays an essential role in diagnosing this condition that radiologists and clinicians should be well aware of. The extent of reversibility depends on how quickly diagnosis is made and how soon the factors favouring development are addressed. Moreover, an understanding of this syndrome must encourage practitioners not to conduct unnecessary repeat imaging when a patient makes good clinical progress.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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